

**REMARKS**

The examiner has requested clarification regarding the structures labeled PNG 6 on page eight of the application. Applicant respectfully requests that the current page eight of the application be replaced with the revised page eight submitted herewith. The corrected page eight contains no new matter.

The compounds as originally labeled referred to two structures as PNG 6, thus making it unclear which structure PNG 6 actually was (on page eight of the application, the compounds were originally labeled as: PNG 2, 6; PNG 3, 7; PNG 4, 8; Z-PNG 4, 9; and PNG 6, 10). The second number of each label was mistakenly included in the application filing as a remnant from an earlier document in which the second number referred to the number of the structure as it occurred in the document itself (i.e. in the case of PNG 2, 6, the six referred to the structure as the 6<sup>th</sup> structure shown in the document overall).

In the correction to the compound labels, the second number of each label has been removed, thereby eliminating the second reference to PNG 6. Corrected page eight compounds are now labeled as: PNG 2; PNG 3; PNG 4; Z-PNG 4; and PNG 6.

Attached to this response, please find the following items:

- 1) Page eight of the original application showing compounds with the original labels.
- 2) Replacement page eight of the application showing compounds with the corrected labels.
- 3) Reference Copy of the USPTO Office Communication (mailed June 26, 2008).

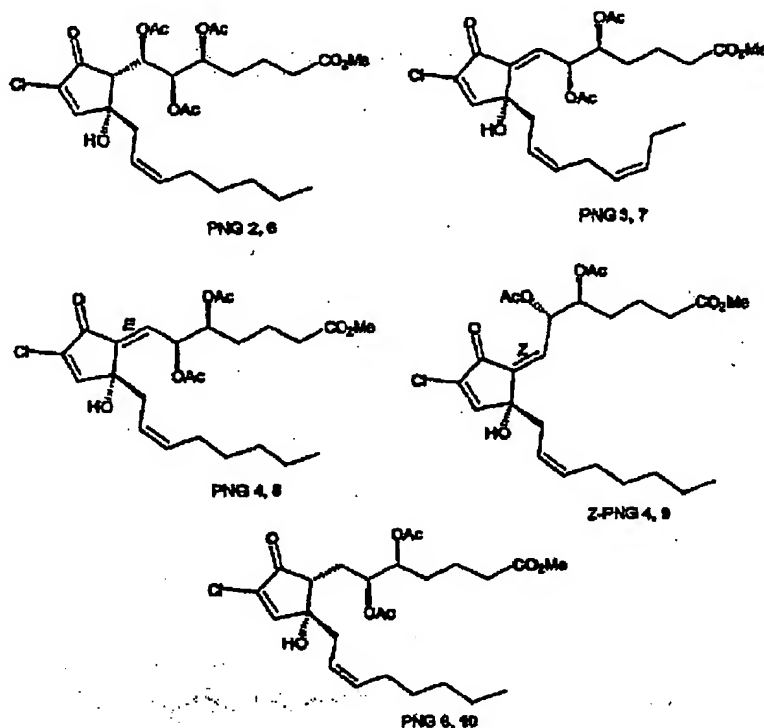
Respectfully submitted,

*July 25, 2008*  
Date

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PCT/US2003/022576

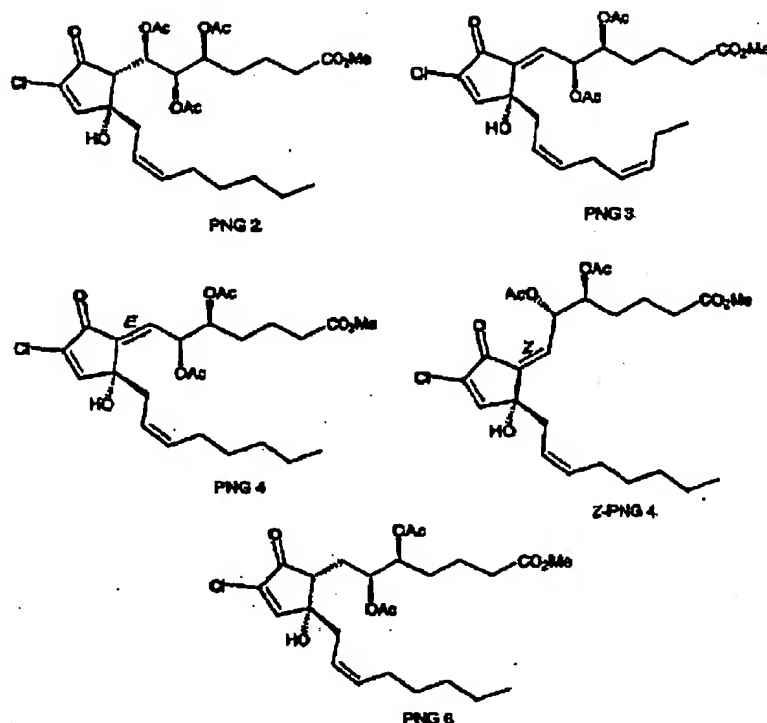


In another embodiment, the inhibitor is selected from the group consisting of cross-conjugated  $\alpha,\beta$ -unsaturated ketones having two sterically unhindered  $\beta$  carbons. The ketone may be a cross-conjugated cyclopentadienone, such as the diterpene shikoccin (NSC-302979), or may be an acyclic compound such as dibenzylideneacetone (DBA), or curcumin. The skilled artisan will recognize that additional compounds containing the pharmacophore also will be active as isopeptidase inhibitors, for example, rabdolatifolin and shikodomedin (Paquette *et al.*, *J. Amer. Chem. Soc.* 118:11990 (1996); *Id.*, 119:9662 (1997)) and O-methyl shikoccin. Shikoccin epoxide and O-methyl shikoccin epoxide (where the endocyclic double bond is replaced by an epoxide) also inhibit endopeptidase activity. In shikoccin epoxide and related compounds the  $\beta$ -carbon still is electrophilic by virtue of the strain of the epoxide ring.

The skilled artisan will further recognize that derivatives of these compounds that retain the pharmacophore identified above also will be active as isopeptidase inhibitors. These compounds may be used alone or in combinations, and may also be used in combination with cyclopentenone prostaglandins of the J series. These compounds are known in the art or can be prepared using known

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,570	11/07/2005	James E Mullally	007180-69 US	4192
36234 7590 06/26/2008 THE MCCALLUM LAW FIRM, P. C. 685 BRIGGS STREET PO BOX 929 ERIE, CO 80516			EXAMINER PAGONAKIS, ANNA	
			ART UNIT 1614	PAPER NUMBER
			MAIL DATE 06/26/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.



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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10521570	11/7/2005	MULLALLY, JAMES E	007180-69 US

THE MCCALLUM LAW FIRM, P. C.  
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EXAMINER

ANNA PAGONAKIS

ART UNIT	PAPER
1614	20080616

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

#### DETAILED ACTION

The reply filed on 3/31/2008 is not fully responsive to the prior Office Action because of the following omission(s) or matter(s): Applicant has elected PNG 6, however, it is not clear which structure this is (please see page 8 where two compounds are labeled as PNG 6). See 37 CFR 1.111. Since the above mentioned reply appears to be bona fide, applicant is given ONE (1) MONTH or THIRTY (30) DAYS from the mailing date of this notice, whichever is longer, within which to supply the omission or correction in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.135(a).

#### Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anna Pagonakis whose telephone number is 571-270-3505. The examiner can be normally reached Monday thru Thursday, 9 am to 5 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access on to Private Pair system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free). If you would like assistance from a USPTO Customer Service Representative or access to be automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ardin Marschel/  
Supervisory Patent Examiner, Art Unit 1614

/Anna Pagonakis/  
Examiner, Art Unit 1614

PTO-80C (Rev.04-03)